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The acute effects of eccentrically-biased versus conventional weight training in older adults: A randomised controlled cross-over study

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Running title: Weight training in older adults

ABSTRACT

Background: Whilst resistance training has been proven to convey considerable benefits to older people; immediately post-exercise there may be elevated transient risks for cardiac events and falls.

Objectives and Measurements: We assessed the acute effects of eccentrically-biased (EB) and conventional (CONV) resistance exercise on: platelet number, activation and granule exocytsosis; and mean velocity of centre of pressure displacement (Vm).

Design, Setting, Participants and Intervention: Ten older adults (7 males, 3 females; 69 ± 4 years) participated in this randomised controlled cross-over study in which they performed EB and CONV training sessions that were matched for total work and a control condition.

Results: Immediately post-exercise there was a statistically significant difference in platelet count between the control condition, in which it fell (pre 224 ± 35 10^9/L; post 211 ± 30 10^9/L: $P < 0.05$) and CONV in which it increased (pre 236 ± 55 10^9/L; post 242 ± 51 10^9/L: $P > 0.05$). There was no change in platelet activation and granule exocytsosis or Vm following EB and CONV.

Conclusions: Overall, while minor differences between regimens were observed, no major adverse effect on parameters of platelet function or centre of pressure displacement were observed acutely following either regimen. Eccentrically-biased and conventional resistance exercise training regimens do not appear to present an elevated acute risk in the context of changes to platelet function contributing to a cardiac event or postural stability increasing falls risk for apparently healthy older adults.

Running title: Weight training in older adults

Key words: Resistance exercise, Platelets, Postural control

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INTRODUCTION

The benefits of conventional (CONV) and eccentrically-biased (EB) resistance training for older adults are well-established,[1-3] Consequently, resistance training is now advocated as an important component of exercise programs for older adults to maintain their health and physical function.[4] However, there is some evidence to suggest that older adults may be at an increased risk of adverse cardiovascular events and debilitating falls due to fatigue immediately after a training session.[5-13].

With regards to increased risk of cardiovascular events immediately post resistance exercise, the incidence of acute myocardial infarction and sudden death after exercise is highest among those who are least physically active.[14] Additionally, since ageing is associated with a decrease in physical activity [1] and an increased prevalence of cardiovascular disease,[15] such risks may be of particular concern when encouraging older adults to commence an exercise program. And whilst older adults may present the greatest risk, it also has implications for the wider population, since such events have also been reported in apparently healthy young adults.[16] Consequently it is important to better understand the potential acute risks of resistance exercise, so as to inform future exercise prescription.

Blood platelets play a critical role in atherothrombotic events, such as heart attack and stroke, with an increased platelet activation or responsiveness to stimulation being associated with an increased risk of acute cardiovascular events.[17] A small number of studies have reported increased platelet reactivity and activation after conventional resistance exercise in young healthy adults.[5, 6] However, there have been no studies to date investigating the acute effects of a resistance training session on platelet function in older adults. Therefore, in this study, platelet activation was measured by the percentage of platelets expressing activated glycoprotein (GP) IIb-IIIa by means of flow cytometry. This glycoprotein is present on the surface of all platelets, but in its activated form, plays an important role in platelet-to-platelet adhesion. After activation, platelets undergo a process of granule excocytosis, which assists in platelet aggregation through the expression of proteins on the surface of the platelet. One of these proteins, P-selectin, was used in our study as another marker of platelet activation by means of flow cytometry.

In addition to the concerns regarding the acute risk of exercise induced cardiac events, there are also concerns regarding the risk of trips and falls, particularly when people are fatigued after an exercise session. For older people, falls risk is a major concern, particularly with the increased prevalence of osteoporosis in this group, and for whom such fractures are associated with elevated morbidity and mortality risk. Moore, Korff, and Kinzey [12] demonstrated that conventional resistance exercise has an acute negative effect on postural stability in older adults, which may then increase the risk of falls in older adults immediately after a resistance training session. However, whilst there have been a number of studies on conventional resistance training, eccentric resistance training for older adults is a relatively new concept and no studies have assessed the effects of eccentrically-biased resistance exercise on postural control.

The aims of the current study were therefore to determine the acute effects of single sessions of conventional (CONV) and eccentrically-biased (EB) resistance training on: platelet count and function, and postural stability in older adults.

METHODS

Participants

Ten community-dwelling older adults (7 males and 3 females; mean ± S.D. age, 69 ± 4 years; body mass, 71.0 ± 11.5 kg; height, 166.3 ± 9.1 cm) participated in this study. Participants were recruited by means of flyers posted around the University campus and distributed to households in the surrounding local community. Participants were excluded from the study if they had relevant cardiovascular or orthopaedic problems, if they had any conditions that affected platelet function, if they had undertaken any resistance training in the preceding six months or if they were taking any medication that affected platelet function by means of a questionnaire. Written informed consent was obtained from all participants before entry into the study, which was approved by the University Human Research Ethics Committee.

Study Design

A randomised controlled cross-over design was used for this study. Participants attended the laboratory on four occasions in total. A priori power analysis based on the most conservative effect size of 0.28 with regards to platelet activation data from flow cytometry (percentage of platelets positive for PAC1) revealed that 10 participants were needed to obtain statistical power of 0.8.[18] The overall study design is illustrated in Figure 1. During the first session, participants were familiarised with the exercises to be performed during the resistance training sessions. One-repetition maximum (1RM) was then quantified for each exercise to be performed in the training sessions. Participants were given a food diary to record their normal diet the day before and on the morning of the first trial session. They were then instructed to replicate this diet for the subsequent two trial sessions. Participants were also instructed to avoid fatiguing physical activity during the 48 hours prior to trial sessions. After a 14 day washout period, participants returned to the laboratory for the first trial session. Before the start of this session, participants were randomised to one of three conditions: CONV, EB or control. This was done by an investigator picking out three pieces of paper, with one condition written on each paper, in random order one at a time from an opaque container. Thus, participants were allocated to the sequence of conditions according to the sequence in which the pieces of paper were picked out. Participants reported to the laboratory for the trial sessions between 7:00am and 8:00am and details of the trial sessions are provided in Figure 2. Blood samples were obtained at each data collection timepoint, followed by measurement of postural control. During the subsequent two trial sessions, the testing protocol was replicated and participants were randomised to the remaining conditions.

Resistance Training

The resistance training sessions consisted of four exercises: 45º leg press, toe press, bench press and latissimus dorsi pulldowns. Detailed description of each exercise has been previously published.[3]

Trial sessions

For the CONV trial, participants performed two sets of each exercise, with three minute rests between sets. Each set involved 10 completely bilateral repetitions at 75% of the 1RM. For the EB trial, participants performed three sets of each exercise, with three minute rests between sets. Each set involved 10 concentric lifts performed bilaterally with 50% of the 1RM. Participants then lowered the weight unilaterally, alternating between left and right limbs with each repetition, thus performing five unilateral eccentric contractions per limb per set. The difference in the number of sets employed in CONV and EB trials in the current study was necessary to match the total volume of work performed by each training group.[3] The training protocols were designed to ensure that participants performed the same amount of work for each limb relative to individual 1RMs in EB and CONV (see Table 1). Actual total concentric work for each limb was calculated by multiplying the actual relative intensity (% of 1RM) by the number of repetitions performed in each set, then summing concentric work performed in each set over the whole training period. Actual total work (concentric and eccentric) for each limb was calculated by multiplying actual concentric work by 2.

The control condition involved participants sitting quietly in the laboratory for 45 minutes.

Table 1

Training method	Contraction mode	Sets	Reps	Relative Intensity[1]	Volume-load[2]
CONV	Concentric	2	10	75%	1500
	Eccentric (bilateral)	2	10	75%	1500
EB	Concentric	3	10	50%	1500
	Eccentric (unilateral)	3	5	100%	1500

CONV = conventional weight training; EB = eccentrically-biased training
1 Relative intensity = % of 1RM
2 Volume-load = sets × repetitions × relative intensity

Blood Sample Collection

At each blood sample collection timepoint a total of 16 ml of venous blood was collected from the antecubital vein into tri-potassium ethylene-diamine-tetra acetic acid (EDTA 1.8 mg/ml) and tri-sodium citrate (3.8%) tubes using a 21-gauge needle. Care was taken to avoid platelet activation while drawing blood samples.[19]

Platelet Activation and Granule Exocytosis

Circulating platelet activation (as measured by glycoprotein (GP) IIb-IIIa activation) and granule exocytsosis (as measured by P-Selectin expression) were assessed by whole blood flow cytometric methods as previously described. [19, 20] Briefly, within 10 min of blood collection whole blood was diluted 1:5 with HEPES saline (10 mM HEPES, 0.15 M NaCl, pH 7.3-7.4). In preparation for flow cytometry, blood was mixed with or without positive control of 50 µM and thrombin receptor activating peptide 6 (TRAP-6) (Sigma, USA) and an antibody cocktail containing 0.5 µg/mL tandem phycoerythrin-cy5 (PC5) conjugated anti-CD42b monoclonal antibody (Becton Dickinson Pharmingen), 0.5 µg/mL fluorescein isothiocyanate (FITC) conjugated PAC-1 (Becton Dickinson, Australia) with or without blockade by 2 µg/mL eptifibatide (Schering-Plough, NSW), and phycoerythrin (PE) conjugated anti-CD62P monoclonal antibody or 1 µg/mL PE conjugated mouse IgG1κ isotypic control for 15 min and the reaction stopped with 800 µL of 1% formaldehyde (Sigma) in HEPES-Saline pH 7.3.

Samples were protected from light and stored at 4 °C until same-day flow cytometry analysis. Platelets were identified by double gating on characteristic forward and side laser scatter properties and expression of the platelet-specific marker CD42b. 10,000 platelet events recorded and the percentage of platelets expressing activated GPIIb-IIIa (as reported by PAC-1 binding greater than eptifibatide-blocked negative control) and P-Selectin expression (as reported by anti-CD62P fluorescence greater than isotypic control) were recorded.

Platelet Count

Blood samples collected in EDTA tubes were analysed for platelet count using an automated differential cell counter (Coulter AcT 5 Diff CP, Coulter Electronics Inc, Hialeah, Florida, USA). Platelet count was corrected for plasma volume [21] to account for hydration status. Coefficients of variation, calculated using the baseline data from the three conditions (EB, CONV and control) for platelet count was 0.79%.

Postural Stability

Details of this method of measuring postural stability have been previously published.[21] Breifly, participants stood quietly barefoot on a force-plate (Kistler Type 9286AA, Kistler Instruments, Winterthur, Switzerland) with their arms comfortably by their sides, their eyes fixed on a point in front of them, their feet abducted 10º and their heels separated medio-laterally by a distance of 6cm. Markings were made on the surface of the force plate to standardise the position of the feet.[22] The force-plate was used to obtain the coordinates of the centre of pressure (COP) in the medial-lateral (x) and anterior-posterior (y) directions. Each trial lasted for 30s and data were sampled at a rate of 100Hz and stored on computer (BioWare 3, Kistler Instruments, Winterthur, Switzerland).

Statistical Analyses

Normality of the data was assessed using the Kolmogorov-Smirnov test, and non-normal data were natural log-transformed. Two-tailed paired samples t-tests were used to compare work done for each exercise and total work done in CONV and EB. Two-way (condition * time) repeated measures analyses of variance (ANOVA) were used to compare EB, CONV and the control condition for platelet activation, platelet count and postural stability. Post-hoc tests with a Bonferroni correction were used to further analyse significant main interactions. Data are presented as mean ± standard deviation (SD). Results were considered significant at $P < 0.05$, and statistical analyses were performed using IBM SPSS Statistics 19.0 (IBM, Somers, NY).

RESULTS

Resistance Training Data

The estimates of amount of work performed in each exercise and total amount of work did not differ significantly between CONV and EB (see Table 2). Although the study was designed to match total work between CONV and EB, the actual work performed differed slightly between conditions due to some participants being unable to complete all 10 repetitions in a set or due to the smallest available weight increment being 1.25 kg for a certain exercise resulting in slightly less or more weight being used than the exact 75% or 100% 1RM.

Table 2

Estimates of mean work overall and for each exercise

	Group	Work (A.U.)	*P*-value
Leg press	CONV	3000 ± 0	-
	EB	3000 ± 0	
Toe press	CONV	3009 ± 28	0.34
	EB	3000 ± 0	
Bench press	CONV	2876 ± 170	0.06
	EB	3168 ± 332	
Lat pulldown	CONV	2972 ± 101	0.91
	EB	2967 ± 105	
Overall	CONV	11857 ± 229	0.09
	EB	12134 ± 359	

CONV = conventional resistance training; EB = eccentrically-biased training; A.U. = arbitrary units. *P*-values are for two-tailed paired *t*-tests performed to compare work performed in EB and CONV. Dash indicates that *t*-test was not performed as values in EB and CONV were identical.

Platelet Number and Function

Platelet count data are summarised in Table 3. Data from nine participants were analysed due to inability to obtain blood samples from one participant. There was no significant difference ($P > 0.05$) in platelet count at baseline between the three conditions. A significant condition by time effect ($P < 0.05$) was observed.

Post-hoc tests revealed that platelet count in the control condition decreased significantly ($P < 0.05$) from baseline to immediately post-control while not changing significantly in CONV ($P = 0.30$) or EB ($P = 0.15$). Platelet count was significantly higher ($P < 0.05$) in CONV than in the control condition immediately post resistance training. Mean platelet count immediately after EB was also higher than the control condition, but this difference was not statistically significant ($P = 0.07$).

Circulating parameters of platelet activation (as measured by PAC-1 binding) and granule exocytosis (as measured by P-selectin expression) as measured by whole blood flow cytometry are presented in Table 3. Platelet activation and granule exocytosis in response to the positive control of TRAP-6 is also presented in Table 3. Data from eight participants were analysed due to sample haemolysis. There was no significant difference ($P > 0.05$) in percent of PAC-1 or P-Selectin positive platelets at baseline between the three conditions. No significant condition ($P = 0.22$), time ($P = 0.42$) or condition by time ($P = 0.71$) effect was observed for percent platelets positive for PAC-1. No significant condition ($P = 0.79$), time ($P = 0.77$) or condition by time ($P = 0.79$) effect was observed for percent platelets positive for CD62P.

Postural Stability

Mean velocity of COP data is summarised in Table 3. There was no significant difference ($P > 0.05$) in Vm at baseline between the three conditions. No significant condition ($P = 0.64$), time ($P = 0.85$) or condition by time ($P = 0.53$) effect was observed for mean velocity of COP.

Table 3

Changes in mean displacement velocity of centre of pressure, platelet count and platelet activation

	Condition	Baseline	Post 0
Vm $\times 10^{-3}$ (m/s)	CONV	2.8 ± 1.1	3.2 ± 1.2
	EB	3.1 ± 1.2	3.0 ± 1.3
	Control	2.9 ± 1.3	2.8 ± 1.1
Platelet count (10^9/L)	CONV	236 ± 55	242 ± 51$^{¥}$
	EB	224 ± 35	233 ± 30
	Control	224 ± 35	211 ± 30*
% Positive NA PAC-1	CONV	7.6 ± 4.6	7.7 ± 5.2
	EB	6.6 ± 7.5	6.8 ± 3.8
	Control	4.7 ± 3.2	5.9 ± 5.4
% Positive NA CD62P	CONV	2.6 ± 1.6	2.8 ± 2.3
	EB	2.9 ± 4.0	2.3 ± 1.5
	Control	2.8 ± 1.9	2.5 ± 1.6
% Positive TRAP PAC-1	CONV	99.0 ± 0.7	
	EB	99.1 ± 0.5	
	Control	98.7 ± 1.0	
% Positive TRAP CD62P	CONV	87.4 ± 11.4	
	EB	88.3 ± 10.1	
	Control	88.3 ± 14.7	

Data presented as mean ± SD; Vm = mean velocity of centre of pressure; % Positive NA PAC-1 = percentage of platelets expressing activated GPIIb-IIIa without positive control or blockade. % Positive NA CD62P = percentage of platelets with P-Selectin expression without positive control or blockade. % Positive TRAP PAC-1 = percentage of platelets expressing activated GPIIb-IIIa with positive control. % Positive TRAP CD62P = percentage of platelets with P-Selectin expression with positive control. Post 0 = immediately post training; Asterisks indicate significant difference from baseline (*P < 0.05). ¥ indicates a significant difference between CONV and control (P < 0.05).

DISCUSSION

To the knowledge of the authors, the current study is the first to compare the acute effects of eccentrically-biased and conventional resistance exercise on platelet function and count, and postural stability in older adults. The baseline data for platelet aggregometry and count and mean velocity of COP displacement parameters agree well with those observed in previous studies.[5, 22]

The finding of a difference in platelet count between the control condition and the two exercise conditions (EB and CONV) post exercise (Post 0) appears to agree with the results of previous studies that demonstrated an increase in platelet count following resistance exercise.[5, 6, 23] However, in this study it should be noted that about two-thirds of the difference post-exercise may be attributed to a decline in the control condition and only about one-third of the difference from an increase in the exercise conditions. Therefore, it could be interpreted that the higher platelet count in the exercise conditions as compared to the control condition post exercise was largely due to the significant decrease during the control condition rather than an increase in platelet count during the exercise conditions per se. This observation is difficult to explain since there is no major diurnal variability in platelet count,[24] and the potential effects of change in hydration have been accounted for. One potential explanation may be that reduced circulation when participants in the control group sat quietly led to accumulation of platelets in non-circulating pools, such as the spleen; whereas all platelets remained circulating in the exercise groups. Although a higher platelet count may be associated with cardiovascular disease,[25] the effect seen is unlikely to be of clinical significance. Heavy resistance exercise is generally well-tolerated among older adults and in this study only a small and non-statistically significant increase was recorded, which further supports the notion that the acute risks appear to be small and when related to the evidence from chronic training studies suggests that the benefits of resistance training outweigh the risks.[4, 14]

We did not observe any significant increase in circulating platelet activation or granule exocytosis as measured by whole blood flow cytometry, a method that is not affected by platelet count.[20] To the knowledge of the authors, there have been no previous studies investigating the effects of resistance exercise on platelet activation by means of flow cytometry. This means that platelet function is not likely to be adversely affected by resistance exercise in older adults.

The finding that the mean velocity of centre of pressure did not change significantly after CONV or EB is in contrast to that observed by Moore et al.,[12] who reported a decline in postural control immediately after resistance exercise in older adults. However, the training protocol employed by Moore et al. [12] consisted of six exercises, all for the legs, and designed to fatigue the leg muscles. In contrast, the resistance training protocol employed in the current study was designed to replicate a typical resistance training session an older adult may undertake for muscle mass and strength gain. The current exercise volumes are more realistic and have proven effective in increasing strength in this older population.[3] Therefore, the training protocol in the current study may have led to less fatigue of the leg muscles than the training protocol employed by Moore et al.,[12] thereby explaining the lack of a significant change in Vm after CONV and EB.

One limitation of the current study is that it is slightly underpowered, as the required number of participants was not achieved for the measures of platelet count, activation and granule exocytosis. However, the current study was powered to show an effect size of 0.28 or greater. Therefore, it could be speculated that while the current study cannot rule out effect sizes smaller than 0.28, it is unlikely that such small effect sizes would be of clinical significance.

Conclusion

Overall, the results suggest that conventional and eccentrically-biased resistance exercise do not seem to have acute-post-exercise clinically relevant effects on platelet function or postural stability in older adults. However, the possibility of better-maintained platelet count after both training modalities mean that more research is needed to fully understand the acute effects of these modalities in older adults.

FIGURE LEGENDS

Figure 1. Overall study timeline. EB = eccentrically-biased resistance training; CONV = conventional resistance training; 1RM = one-repetition maximum test.

Figure 2. Trial timeline. EB = eccentrically-biased resistance training; CONV = conventional resistance training.

Figure 1.

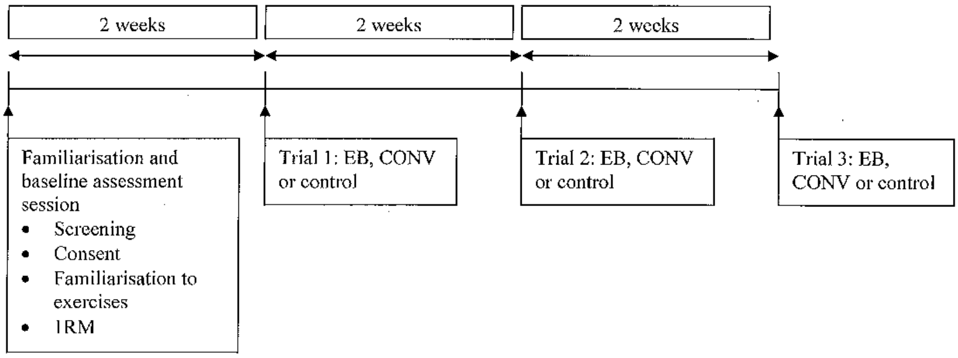
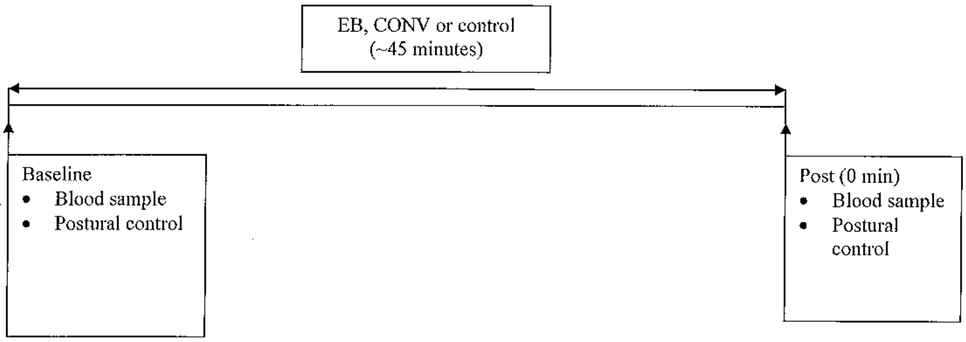

2 weeks
2 weeks
2 weeks
Familiarisation and baseline assessment session
• Screening
• Consent
• Familiarisation to exercises
• 1RM
Trial 1: EB, CONV or control
Trial 2: EB, CONV or control
Trial 3: EB, CONV or control

Figure 2.


EB, CONV or control
(~45 minutes)
Baseline
Blood sample
Postural control
Post (0 min)
Blood sample
Postural
control

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Author Contributions

Isaac Selva Raj: Substantial contribution to study concept and design, acquisition of data, analysis and interpretation of data. Drafted article for publication and approved final version to be published.

Ben A. Westfold and Matthew D. Linden: Substantial contribution to study concept and design, acquisition of data, analysis and interpretation of data. Revised draft article for important intellectual content and approved final version to be published.

Anthony J. Shield and Stephen R. Bird: Substantial contribution to study concept and design, analysis and interpretation of data. Revised draft article for important intellectual content and approved final version to be published.

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REFERENCES

1 Doherty TJ. Invited review: Aging and sarcopenia. *J Appl Physiol* 2003;**95**(4):1717-27.

2 Macaluso A, De Vito G. Muscle strength, power and adaptations to resistance training in older people. *Eur J Appl Physiol* 2004;**91**(4):450-72.

3 Raj IS, Bird SR, Westfold BA, et al. Effects of eccentrically biased versus conventional weight training in older adults. *Med Sci Sports Exerc* 2012;**44**(6):1167-76.

4 Chodzko-Zajko WJ, Proctor DN, Fiatarone Singh MA, et al. American College of Sports Medicine position stand. Exercise and physical activity for older adults. *Med Sci Sports Exerc* 2009;**41**(7):1510-30.

5 Ahmadizad S, El-Sayed MS. The effects of graded resistance exercise on platelet aggregation and activation. *Med Sci Sports Exerc* 2003;**35**(6):1026-32.

6 Ahmadizad S, El-Sayed MS, Maclaren DP. Responses of platelet activation and function to a single bout of resistance exercise and recovery. *Clin Hemorheol Microcirc* 2006;**35**(1-2):159-68.

7 Barnes JN, Trombold JR, Dhindsa M, et al. Arterial stiffening following eccentric exercise-induced muscle damage. *J Appl Physiol* 2010;**109**(4):1102-8.

8 Collier SR, Diggle MD, Heffernan KS, et al. Changes in arterial distensibility and flow-mediated dilation after acute resistance vs. aerobic exercise. *J Strength Cond Res* 2010;**24**(10):2846-52.

9 DeVan AE, Anton MM, Cook JN, et al. Acute effects of resistance exercise on arterial compliance. *J Appl Physiol* 2005;**98**(6):2287-91.

10 Heffernan KS, Jae SY, Edwards DG, et al. Arterial stiffness following repeated Valsalva maneuvers and resistance exercise in young men. *Appl Physiol Nutr Metab* 2007;**32**(2):257-64.

11 Yoon ES, Jung SJ, Cheun SK, et al. Effects of acute resistance exercise on arterial stiffness in young men. *Korean Circ J* 2010;**40**(1):16-22.

12 Moore JB, Korff T, Kinzey SJ. Acute effects of a single bout of resistance exercise on postural control in elderly persons. *Percept Mot Skills* 2005;**100**(3 Pt 1):725-33.

13 Singh NB, Arampatzis A, Duda G, et al. Effect of fatigue on force fluctuations in knee extensors in young adults. *Philos Transact A Math Phys Eng Sci* 2010;**368**(1920):2783-98.

14 Thompson PD, Franklin BA, Balady GJ, et al. Exercise and acute cardiovascular events placing the risks into perspective: a scientific statement from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism and the Council on Clinical Cardiology. *Circulation* 2007;**115**(17):2358-68.

15 Roger VL, Go AS, Lloyd-Jones DM, et al. Heart disease and stroke statistics--2012 update: a report from the American Heart Association. *Circulation* 2012;**125**(1):e2-e220.

16 Bernard F, Schiano P, Ollivier JP. [Coronary dissection associated with exercise: unusual cause of myocardial infarction]. *Archives des maladies du coeur et des vaisseaux* 2003;**96**(10):995-7.

17 Linden MD, Furman MI, Frelinger AL, 3rd, et al. Indices of platelet activation and the stability of coronary artery disease. *J Thromb Haemost* 2007;**5**(4):761-5.

18 Faul F, Erdfelder E, Lang AG, et al. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods* 2007;**39**(2):175-91.

19 Linden MD, Frelinger AL, 3rd, Barnard MR, et al. Application of flow cytometry to platelet disorders. *Semin Thromb Hemost* 2004;**30**(5):501-11.

20 Michelson AD, Linden MD, Barnard MR, et al. Flow Cytometry. In: Michelson AD, editor. Platelets. San Diego: Academic Press; 2007.

21 Dill DB, Costill DL. Calculation of percentage changes in volumes of blood, plasma, and red cells in dehydration. *J Appl Physiol* 1974;**37**(2):247-8.

22 Raymakers JA, Samson MM, Verhaar HJ. The assessment of body sway and the choice of the stability parameter(s). *Gait Posture* 2005;**21**(1):48-58.

23 Ahmadizad S, El-Sayed MS, MacLaren DP. Effects of time of day and acute resistance exercise on platelet activation and function. *Clin Hemorheol Microcirc* 2010;**45**(2-4):391-9.

24 Akkok CA, Hervig T, Bjorsvik S, et al. Minor diurnal and activity-induced variations in daytime peripheral blood platelet counts do not have any major impact on platelet yield by platelet apheresis. *Transfus Apher Sci* 2010;**43**(1):33-6.

25 El-Sayed MS, Ali N, El-Sayed Ali Z. Aggregation and activation of blood platelets in exercise and training. *Sports Med* 2005;**35**(1):11-22.